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PRINCIPAL INVESTIGATOR: Linda S. Cook, Ph.D.

CONTRACTING ORGANIZATION: Fred Hutchinson Cancer Research Center
Seattle, Washington 98104-2092

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Linda S. Cook, Ph.D.

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Fred Hutchinson Cancer Research Center
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13. ABSTRACT *(Maximum 200 words)*

This grant funded postdoctoral training for Dr. Cook's analyses investigating risk factors for breast cancer. Briefly, we found a small elevation in breast cancer risk associated with any use of hair coloring, although exclusive use of one of the four types of hair coloring application was not associated with elevated risks among reproductive-age women. Elevations in risk were not restricted to one type of hair coloring application (for example rinses or frosting) in combination with the other types. Hair spray use was not associated with an elevation in risk. Another analysis suggested that among multiparous women of the same age, parity, and age at first term birth, there was no increased risk of breast cancer for those who had their last term pregnancy late in their reproductive life compared to women who had their last term pregnancy earlier. Our results also suggested no consistent pattern of an elevated risk for breast cancer for several years following a term birth for women who have another pregnancy compared to women of the same age who do not have an additional pregnancy. Results concerning the relation between occupation and breast cancer risk in young women are pending review and approval by other investigators.

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Linda S. Cook 7/29/98

PI - Signature Date

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Introduction

The U.S. Army Medical Research and Materiel Command under DAMD-14-96-1-6118 provided funding for two years of postdoctoral training to support Dr. Cook's work on analyses involving the epidemiology of breast cancer in women. The proposed analyses used data from three population-based case control studies that collected detailed information on many factors known, or suspected to be, related to the risk of breast cancer. These analyses evaluated hypotheses of scientific and public health interest that were not identified as specific aims in the original grant protocols. The proposed analyses were designed explore the relationship between various reproductive, lifestyle, and occupational exposures and breast cancer risk for which inconsistent or inconclusive associations have been reported.

In the original proposal we asked for three years of funding to complete these analyses but were provided with two years of funding which ended June 30, 1998. (Please note that in the Annual Report Review for the reporting period July 1996 to June 1997, the reviewer evaluated the statement of work [SOW] under 'contractual issues' as if Dr. Cook was funded for three years. A copy of this Annual Report Review is included in the Appendix for reference.) Three of the four proposed analyses have been completed. Although an effort was made to complete all analyses in the two years of funding, the analysis evaluating whether various aspects of lactation are associated with a decrease in breast cancer risk was not completed in the allotted time period. The following analyses have been completed (or just require finishing touches) and have been summarized in manuscripts that are in varying stages of completion (from submitted manuscripts to working drafts):

1. the risk of breast cancer related to personal hair dye use among young women,
2. the risk of breast cancer related to a recent term pregnancy,
3. the risk of breast cancer related to different types and groupings of occupations, as well as presumed exposure to electromagnetic fields and strenuous physical activity.

Progress Report

The purpose, contribution, and status of each analysis/manuscript are indicated below.

1. Hair dye use:

This analysis evaluated whether or not hair dye use increases breast cancer risk among young women. The results of this analysis were presented at the 30th annual meeting of the Society for Epidemiologic Research (SER) in Edmonton, Alberta (June 1997). A manuscript related to this analysis is under peer-review; thus, to honor journal related embargoes, the following includes the results and discussion as presented at the SER meeting. (Please note that this is the same summary as that provided in the Annual Report for the reporting period July 1996 to June 1997).

Introduction

The reported mutagenic effects of permanent and semi-permanent hair dyes (1) and the carcinogenic effects of some coal-tar derivatives found in hair coloring products (2), has raised concern that personal hair dye use could increase the risk of breast cancer. Early studies that explored this possibility found some modest increases in risk, particularly among subgroups of women (e.g. those with long durations of regular use or among smokers only) (3-8). Later studies found no over-all association with permanent hair dye use or the duration of use (9-14). However, the majority of women in the later studies were 50 years of age or older. In this population-based case control study, information on the type, duration, and frequency of hair coloring application was collected to evaluate the impact of hair coloring on the risk of breast cancer among reproductive-age women.

Methods

Eligible case women included white women residing in three counties of western Washington who were diagnosed with insitu or invasive breast cancer between 1983 and 1990 and who were born in 1945 or later. Thus, all case women were 21-45 years of age. These women were identified through the Cancer Surveillance System of western Washington, a participant in the National Cancer Institute's Surveillance, Epidemiology, and End Results Program. After obtaining written, informed consent, 83.6% of the eligible case women were successfully interviewed. We excluded one woman with unknown hair coloring application, leaving 844 women available for analysis (n=97 in-situ and n=747 invasive cases).

Women of similar age, who lived in these counties and were identified by random digit dialing, served as controls. 97% of residences were successfully screened and after obtaining written, informed consent, 78.0% of eligible control women were successfully interviewed. We excluded one woman with unknown hair coloring application, leaving 960 control women for analysis.

The women completed a structured, in-person interview and provided information on demographic and lifestyle characteristics, as well as reproductive and medical histories. Additionally, women were queried about hair coloring application. Those who answered affirmatively were further questioned about their natural hair color, the types of hair coloring used, the desired color results, the frequency of application, and the amount of time the coloring product remained on their hair to achieve the desired result. Types of hair coloring were recorded under five categories: rinses (coloring applied to hair that washed out the next

shampoo), semi-permanent dyes (coloring that remained over multiple washings), permanent dyes (coloring never washed out), bleaching then dyeing with either semi-permanent or permanent dyes, or frosting/tipping (partial coloring of hair). In the present analysis semi-permanent and permanent dye use was combined since the results for each analysis separately were very similar. Women were also queried about using hair spray, and for those that used hair spray, the frequency of use. Information on hair spray use was available for 770 (91.2%) of the 844 breast cancer cases and all control women.

Results

Apart from hair coloring application, the distribution of other characteristics of our cases and controls was consistent with the known or suspected factors influencing breast cancer risk among young women. For example, cases women were slightly more likely to be nulliparous than control women and much more likely to have a family history of breast cancer in a first degree relative. These characteristics along with weight were also related to hair coloring application. All odds ratios presented in this analysis are adjusted for age, parity, weight, and a family history of breast cancer in a first degree relative. Further adjustment for education, income, religious affiliation, marital status, height, oral contraceptive use, age at menarche, age at first fullterm birth, or smoking and alcohol consumption did not alter the estimated odds ratios.

For all the relative risk estimates reported in the present analysis, women who reported any method, type, or frequency of hair coloring application were compared to women who stated they had never colored their hair - a group consisting of 315 breast cancer cases and 418 controls. Slightly more cases than controls, 62.7% vs. 56.5% respectively, reported some type hair color application, resulting in a small elevation in the risk for breast cancer (Table 1). However, there was no increasing risk with increased frequency of use, illustrated here by the total lifetime episodes of hair coloring application, and no elevation in risk for the large number of women who had colored their hair within 4 years of reference date.

Table 1. Hair coloring application and the risk of breast cancer.

	Cases (n)	Controls (n)	Adjusted OR*	(95% CI)
Use of hair coloring :				
none	315	418	1.00	referent
any	529	542	1.28	(1.05, 1.56)
Total lifetime episodes: 1 - 2	108	126	1.23	(0.91, 1.67)
3 - 9	130	142	1.21	(0.90, 1.62)
10 - 34	140	132	1.40	(1.05, 1.88)
$\geq$ 35	140	138	1.29	(0.97, 1.73)
Time since last use: $\leq$ 4 yrs	304	330	1.19	(0.95, 1.49)
5 - 14 yrs	123	105	1.64	(1.21, 2.24)
$\geq$ 15 yrs	101	106	1.20	(0.86, 1.65)

* adjusted for age, parity, weight in kilograms, and a family history of breast cancer.

Table 2. Breast cancer risk by specific types of hair coloring use.

	Cases (n)	Controls (n)	Adjusted OR*	(95% CI)
Use of hair coloring :				
none	315	418	1.00	referent
Any rinses	92	66	1.72	(1.19, 2.49)
Only rinses	23	18	1.69	(0.88, 3.26)
Any semi-permanent/permanent	406	424	1.27	(1.02, 1.56)
Only semi-permanent/permanent	254	316	1.06	(0.84, 1.34)
Any bleach then dye	69	39	2.54	(1.64, 3.94)
Only bleach then dye	7	7	1.49	(0.49, 4.47)
Any frosting/tipping	194	167	1.55	(1.19, 2.02)
Only frosting/tipping	63	74	1.15	(0.79, 1.68)

* adjusted for age, parity, weight in kilograms, and a family history of breast cancer.

Table 3. Hair spray use and the risk of breast cancer.

	Cases (n=770)	Controls (n=960)	Adjusted OR*	(95% CI)
Hair spray use:				
none	126	161	1.00	referent
any	640	795	0.99	(0.76, 1.29)
Total lifetime episodes:				
< 400	124	154	1.13	(0.80, 1.60)
401 - 2000	134	187	0.94	(0.67, 1.31)
2001 - 6000	161	236	0.85	(0.62, 1.17)
> 6000	218	215	1.10	(0.80, 1.52)

* adjusted for age, parity, weight in kilograms, and a family history of breast cancer.

Because many women used more than one method of hair coloring application, breast cancer risk was further assessed for those that exclusively used one of the four methods of application and for those that reported any use of the four methods of application (Table 2). Among the small number of women who reported exclusive use of rinses there was a

suggestion of an elevated risk, but the confidence interval is wide and includes the null value. Among those with exclusive use of semi-permanent and/or permanent dyes or exclusive frosting or tipping application there was no elevation in breast cancer risk. The risk for those women who reported first bleaching and then dyeing their hair is not clear since only 7 cases and 7 controls reported this exposure.

We found modest elevations in breast cancer risk for those who reported any use of the four methods of hair coloring application. However, no one type of hair coloring application (for example rinses or frosting) in combination with the other types appeared to account for the elevation in risk (data not shown). Furthermore, we found no increasing risk with increased frequency of use or any consistent pattern of risk associated with the timing of use (data not shown).

Any hair spray use and the total number of times it was applied to hair was not related to the risk of breast cancer (Table 3). This was also true when we examined aerosol sprays and pump sprays separately (data not shown).

Discussion

While our results suggest that the impact, if any, of hair coloring application on breast cancer risk is small, there are several issues that should be considered in the interpretation of our results. Eighty-four percent of eligible cases and 76% of eligible controls participated in our study. If substantial differences in hair color application existed between participating and non-participating women, our study results may over- or under-estimate the true risks for breast cancer.

Additionally, it is not clear how well summary measures of hair color application correctly estimate actual exposure to any particular constituent(s) in these products that may influence breast cancer risk. Women in the present study colored their hair over a period of time from 1953 through 1990, with over 95% of use occurring between 1960 and 1990. The hair coloring formulations changed over this time period and products were also introduced and removed from the consumer market during this time period.

It is also possible that the completeness of the reporting of hair coloring application differed between cases and controls, biasing our relative risk estimates to some degree.

While we found a small elevation in breast cancer risk associated with any use of hair coloring, exclusive use of one of the four types of hair coloring application was not associated with elevated risks for breast cancer among reproductive-age women. It is not clear why we found an elevated breast cancer risk associated with any use of one of the four types of hair coloring application. Elevations in risk were not restricted to one type of hair coloring application (for example rinses or frosting) in combination with the other types. Furthermore, we found no increasing risk with increased frequency of use or any consistent pattern of risk associated with the timing of use. And finally, hair spray use was not associated with an elevation in breast cancer risk.

The results of other studies that have investigated the impact of hair coloring application on breast cancer risk that specifically reported risks for reproductive-age women have been inconsistent; one reported an elevated risk (6), one a suggestion of an elevated risk (11), and one no elevation in risk (10). In our study, the lack of an association between exclusive use of a single type of hair coloring application and breast cancer risk, particularly among the large number of women who exclusively used semi-permanent and permanent dyes, argues

that hair coloring application does not influence breast cancer risk among reproductive-age women. However, we did see a small elevation in breast cancer risk associated with the use of any hair coloring. Thus, we cannot preclude the possibility that there may be a small elevation in breast cancer risk associated with hair coloring application.

If the potential small increased risk for breast cancer is investigated further, the uncertainty associated with reported hair coloring exposures needs to be reduced. Cohort studies with detailed cumulative lifetime exposures would remove subject recall errors and still be able to evaluate details of hair coloring application. Furthermore, toxicological studies of the absorption, metabolisms, and carcinogenic potential of constituents and mixtures of constituents in hair coloring products are needed to establish possible mechanisms of carcinogenesis.

2. Recent term pregnancy

This analysis evaluated whether a term pregnancy increases the risk of breast cancer for some period of time following that pregnancy. The results of this analysis were presented at the Era of Hope meeting of the Department of Defense Breast Cancer Research Program in Washington DC (Oct/Nov 1997). The following includes the results and discussion as presented at the Era of Hope meeting. A manuscript related to this analysis has been drafted, but has not yet been reviewed by all the co-authors. It is possible that there will be changes in the analysis or additional analyses conducted based on the final comments of the co-authors. We expect to have the manuscript submitted to a peer-reviewed journal by the end of the year (December 1998).

Introduction

A term pregnancy, especially early in reproductive life, has consistently been associated with an overall reduced risk of breast cancer. However, the results of some studies suggest that for a period of up to several years following a pregnancy there may be an increase in the risk of breast cancer.

There are different ways to conduct analyses related to a recent term pregnancy depending on the study question that is asked. We asked two questions: first, among women with the same number of term pregnancies, is the risk of breast cancer influenced by how recently the last pregnancy occurred? To answer this question, we evaluated breast cancer risk by the time since last pregnancy among women with two or more births while controlling for the total number of term pregnancies and the age at first childbirth. We also asked, does an additional birth increase a woman's risk of breast cancer compared to a woman who did not go on to have another child, and, if so, for what amount of time? To answer this question, we evaluated breast cancer risk by time since last pregnancy by comparing women of a given number of childbirths to women with one less childbirth. Thus, women of parity 2 were compared to women of parity 1, those of parity 3 with women of parity 2, and so on. The results for these two analyses are presented separately.

Methods

We combined data from two population-based case-control studies of breast cancer conducted in western Washington. The two studies were very similar, differing only in the ages of women included and the diagnosis years of breast cancer. Both studies conducted in-person interviews and the information collected on pregnancies was virtually identical. In

both studies, women newly diagnosed with breast cancer were identified from the Cancer Surveillance System of western Washington, a participant in the National Cancer Institute's Surveillance, Epidemiology, and End Results (or SEER) program. Eighty-four percent and 76%, respectively, of eligible case women were interviewed. Since we were interested in the effects of a recent term pregnancy, we restricted our study population to reproductive-age women, or those less than 45 years of age. Women under the age of 25 were excluded because of small numbers of women in this age group; only 9 cases were between 21 and 24 years of age. In total, 1023 case women were available for analysis. In both studies, control women were identified by random digit telephone dialing. Seventy-six percent and 71%, respectively, of eligible controls were interviewed. After applying the same age restrictions applied to cases, a total of 1116 control women were available for analysis.

Both studies conducted in-person interviews and collected essentially the same information on pregnancies. Women were asked about the outcome of each of their pregnancies (if it resulted in a live birth or a still birth, or a miscarriage, and so on), the date of each pregnancy outcome, and, for each live birth, if the child was breast-fed and for how long. We defined the recency of the last term pregnancy as the amount of time from the birth date of the last term pregnancy to the reference date. The reference date is the date of cancer diagnosis among breast cancer cases and a similar assigned date among the control women.

Results

Table 4 shows selected characteristics of case and control women. The distribution of the total number of term pregnancies was similar between the two groups of women. Very few women, either cases or controls, had four or more term pregnancies.

Table 5 shows the results related to the first study question: among women with the same number of term pregnancies, is the risk of breast cancer influenced by how recently the last pregnancy occurred? In this analysis we only included women with 2 or more term pregnancies, 562 cases and 631 controls. Women with one term pregnancy were excluded to allow adjustment for age at first birth in these analyses. For women with one term pregnancy, reference age minus the age at first birth equals the amount of time since the last birth. Thus, the independent effect of time since last birth cannot be measured in women with one term pregnancy. Using more than 10 years since the last birth as the reference category, we found no variation or elevation in breast cancer risk for women who had their last childbirth in the last 7 to 9 years, 3 to 6 years, or within the last 3 years. The same was true in separate analyses of women who breast-fed with the last term pregnancy, and for those who did not breast feed with the last term pregnancy.

Table 6 show the results related to our second study question: does an additional birth increase a woman's risk of breast cancer and, if so, for what amount of time? Again, to answer this question, we evaluated breast cancer risk by time since last pregnancy by comparing women of a given number of childbirths to women with one less childbirth. Because we had so few women with 4 or more term pregnancies, we only compared women of parity 3 to women of parity 2, those of parity 2 to women of parity 1, and those of parity 1 to nulliparous women. We further stratified these analyses on reference age. Thus, separate analyses were run for each age- and parity-group. In all the comparisons we made there was no consistent pattern of an elevated risk for breast cancer for women with an additional, recent term pregnancy.

Table 4. Selected characteristics of breast cancer cases and controls.

Characteristic	Cases (n = 1023) n	%	Controls (n = 1116) n	%
Age				
25-29	48	4.7	108	9.7
30-34	179	17.5	240	21.5
35-39	407	39.8	408	36.6
40-45	389	38.0	360	32.3
Total pregnancies				
0	180	17.6	181	16.2
1	136	13.3	163	14.6
2	287	28.1	327	29.3
3	230	22.5	223	19.8
4	107	10.5	119	10.7
≥ 5	83	8.1	103	9.2
Total full-term births				
0	278	27.2	277	24.8
1	183	17.9	206	18.5
2	361	35.3	417	37.4
3	150	14.7	146	13.1
4	34	3.3	51	4.6
≥ 5	17	1.7	17	1.5
unknown	0	---	2	0.2
Age at first full-term birth				
no full-term births	278	27.2	277	24.8
<20	133	13.0	174	15.6
20-29	492	48.1	536	48.0
≥ 30	120	11.7	127	11.4
unknown	0	---	2	0.2
History breast cancer in mother/sister(s)				
no	864	84.5	1055	94.5
yes	159	15.5	61	5.5

Table 5. Years since last birth and the risk of breast cancer for multiparous women 25-45 years of age.

Years since last birth	Cases n=562	Controls n=631	RR*	(95%CI)
< 3	78	97	0.96	(0.62, 1.50)
3 - 6	124	159	0.90	(0.63, 1.29)
7 - 9	93	98	0.99	(0.69, 1.42)
≥ 10	267	277	1.00	referent

*: adjusted for age (25-29, 30-34, 35-39, 40-45), age at first birth (<20, 20-30, ≥30), parity (2,3,4,≥5), and a family history of breast cancer in a first degree relative (yes, no).

Table 6. The risk of breast cancer for women with parity N+1 relative to women of parity N among women 25-45 years of age.

Birth number	Years since birth N+1	Age 25 - 34 years Cases n	Controls n	RR*	(95%CI)	Age 35 - 39 years Cases n	Controls n	RR*	(95%CI)	Age 40 - 45 years Cases n	Controls n	RR*	(95%CI)
N=0	N /A	91	135	1.0	referent	108	81	1.0	referent	79	61	1.0	referent
N+1=1	< 3	15	31	0.7	(0.3, 1.3)	13	10	0.9	(0.4, 2.2)	2	4	0.4	(0.1, 2.4)
	3 - 6	12	18	1.0	(0.4, 2.1)	17	9	1.5	(0.6, 3.5)	6	5	1.0	(0.3, 3.3)
	7 - 9	5	8	0.8	(0.3, 2.7)	12	11	0.8	(0.3, 1.9)	4	8	0.3	(0.1, 1.2)
	≥ 10	6	16	0.5	(0.2, 1.3)	45	40	0.9	(0.5, 1.5)	46	46	0.8	(0.5, 1.4)
	any	38	73	0.7	(0.4, 1.2)	87	70	1.0	(0.6, 1.5)	58	63	0.7	(0.4, 1.2)
N=1	N /A	38	73	1.0	referent	87	70	1.0	referent	58	63	1.0	referent
N+1=2	< 3	31	31	1.8	(0.9, 3.5)	29	30	0.3	(0.1, 0.8)	5	5	1.0	(0.3, 3.7)
	3 - 6	24	39	1.4	(0.7, 2.7)	33	43	0.7	(0.4, 1.2)	14	18	0.9	(0.4, 2.0)
	7 - 9	10	12	1.9	(0.7, 4.9)	10	23	0.7	(0.4, 1.3)	19	24	0.9	(0.4, 1.7)
	≥ 10	4	14	0.7	(0.2, 2.7)	64	81	0.7	(0.4, 1.1)	118	97	1.3	(0.8, 2.0)
	any	69	96	1.6	(0.9, 2.6)	136	177	0.6	(0.4, 0.9)	156	144	1.1	(0.7, 1.7)
N=2	N /A	69	96	1.0	referent	136	177	1.0	referent	156	144	1.0	referent
N+1=3	< 3	7	15	0.7	(0.3, 1.9)	13	11	1.7	(0.7, 3.8)	5	0	∞	(0.83,---†
	3 - 6	13	13	1.3	(0.5, 3.0)	16	18	1.2	(0.6, 2.4)	8	8	0.9	(0.3, 2.4)
	7 - 9	3	5	0.6	(0.1, 2.8)	9	7	1.6	(0.6, 4.4)	13	7	1.8	(0.7, 4.7)
	≥ 10	0	2	----	----	20	18	1.3	(0.7, 2.7)	43	42	1.0	(0.6, 1.6)
	any	23	35	0.9	(0.5, 1.7)	58	54	1.4	(0.9, 2.2)	69	57	1.2	(0.8, 1.8)

*: adjusted for age (continuous adjustment within the age categories indicated above), a family history of breast cancer first degree relative (yes, no) and, except for N+1=1 / N=0 comparisons, age at first birth (<20,20-29,30+).

†: lower 95% confidence bound determined for an infinite relative risk .

Discussion

How do our results compare with others? With respect to our first study question (among women with the same number of term pregnancies, is the risk of breast cancer influenced by how recently the last pregnancy occurred?), we added our results to a table presented by Cummings et al (15) (Table 7). All of the analyses included in Table 7 were restricted to women with two or more term pregnancies and were adjusted for age, age at first term pregnancy, and number term pregnancies. Results from population-based studies report very small, if any, increased risk of breast cancer for women who had their last term pregnancy recently compared with women who had their last term pregnancy in the more distant past. Stronger elevations in risk were reported from studies using hospital-based comparison groups. As the authors of these hospital-based studies acknowledge, it is possible that women with a recent term pregnancy might have an artificially low rate of hospitalization, particularly for elective or non-acute procedures, resulting in an exaggerated elevation in breast cancer risk.

Table 7. Relative risk estimates from case-control studies of breast cancer in relation to time since last term pregnancy (adapted from Cummings et al [15]).

	Source of	Years since last term pregnancy			
First author	controls	< 3	3 – 6	7 – 9	> 10*
Bruzzi (16)	Hospital	2.7	1.8	1.4	1.0
Williams (17)	Hospital	2.9	1.4	0.8	1.0
Shapiro (18)	Hospital	0.9	1.2	1.6	1.0
Cummings (19)	RDD†	1.2	1.2	1.0	1.0
Leon (20)	Birth records	1.2	1.1	1.0	1.0
Present study	RDD†	1.0	0.9	1.0	1.0

* : referent category

†: random digit dialing

With respect to the second study question (does an additional birth increase a woman's risk of breast cancer and, if so, for what amount of time?) the different analytical approaches and the differing presentation of results in published studies make it difficult to make direct comparisons between studies. The results of some studies suggest that there may be a short-term increased risk of breast cancer associated with an additional birth for some subgroups of women defined by a combination age, age at first birth, and time since the last birth. However, the particular subgroup(s) of women for whom this would apply is not clear since the results across studies are inconsistent.

Some limitations of our study include the 84 and 76% response among case women and the 76 and 71% response among control women. If substantial differences in parity or the timing of term pregnancies existed between participating and non-participating women, our results may over- or under-estimate the true risks for breast cancer. Additionally, we had small numbers of women in each category of time since last pregnancy in our analyses restricted by age and parity that limited the precision of our results.

In summary, our results suggest that among multiparous women of the same age, parity, and age at first term birth, there is no increased risk of breast cancer for those who had their last term pregnancy late in their reproductive life compared to women who had their last term

pregnancy earlier. Our results also suggest that there is no consistent pattern of an elevated risk for breast cancer for several years following a term birth for women who have another pregnancy compared to women of the same age who do not have an additional pregnancy.

3. Occupation

With the expert assistance of Dr. Paul Demers (Occupational Epidemiologist, University of British Columbia), we investigated the influence of occupational history on breast cancer risk. These analyses were just recently completed (June 1998) and will not be presented in full since some of the researchers involved in the project have not had the opportunity to review the final results. Thus, the following partial draft manuscript will only include a brief summary of the methods and the distribution of occupation/industry, exposure to electromagnetic fields (EMF), and exposure to occupational physical activity among breast cancer cases and control women. We expect to have one or more manuscripts related to this analysis submitted for peer-review publication by the end of the year (December 1998).

Methods

Eligible case women included white women residing in three counties of western Washington who were diagnosed with in-situ or invasive breast cancer between 1983 and 1990 and who were born in 1945 or later. All case women were 21-45 years of age. A total of 1011 women were identified through the Cancer Surveillance System of western Washington, a participant in the National Cancer Institute's Surveillance, Epidemiology, and End Results Program. After obtaining written, informed consent, 84% (n=845) of the eligible case women were successfully interviewed. The remaining 166 women were not interviewed due to death prior to study contact (n=58), patient refusal (n=71), and physician refusal to give permission for patient contact (n=37).

Women of similar age, who lived in these counties and were identified by random digit dialing, served as controls. Ninety-six percent of residences were successfully screened for eligible control women. After obtaining written, informed consent, 78% (n=961) were successfully interviewed, resulting in a final response of 75%.

The women completed a structured, in-person interview and provided information on demographic and lifestyle characteristics, as well as reproductive and medical histories. Additionally, women were queried about the occupation and industry for their three longest held jobs, as well as the start and end date for each reported job. Only work history from the age of 18 or older was considered. All occupations and industries were coded according the 1980 US Census codes. After eliminating persons who did not report paid employment (excluding women who report "employment" solely as a housewife or student), there were 754 cases and 942 controls who reported an average of 2.35 and 2.20 jobs, respectively (Table 8). Among the 3,847 jobs there were 1,453 unique occupation and industry combinations. These jobs were classified into categories of EMF exposure and physical activity without knowledge of case or control status.

Table 8. Number of jobs reported by breast cancer cases and Control women aged 45 years or less.

	Cases (n=754)		Controls (n=942)	
Jobs reported	n	%	n	%
One	128	17.0	212	22.5
Two	234	31.0	327	34.7
Three	392	52.0	403	42.8

Similar occupations (Table 9) and industries (Table 10) were grouped using a program developed by Thomas Vaughan of the Fred Hutchinson Cancer Research Centre. This coding scheme has been used in studies of a variety of cancer sites (21, 22). Because physically demanding work and industrial work may be correlated with socioeconomic status, SES was considered as a possible confounding variable. Each job was classified as to its SES using a revision of Duncan's Socioeconomic Index based on the education and income characteristics of persons holding that occupation from the US census (23). The mean socioeconomic index was 43.1 for case women and 41.7 for control women.

Table 9. Prevalence of ever employment in occupational groups among breast cancer cases and control women.

	Cases		Controls	
Occupational Group	n	Prevalence	n	Prevalence
Admin. & Managerial Occupations	134	17.77%	134	14.23%
Engineers, Architects, Surveyors	8	1.06%	9	0.96%
Mathematical & Computer Scientists	14	1.86%	17	1.80%
Natural Scientists, Except Chemists	3	0.40%	4	0.42%
Chemists & Chemical Technicians	0	0.00%	1	0.11%
Health Diagnosing Occupations	2	0.27%	5	0.53%
Nurses (RN'S & LPN'S)	36	4.77%	58	6.16%
Other Health Treatment Occupations	13	1.72%	20	2.12%
Educators, Librarians, Educ. Counselors	112	14.85%	137	14.54%
Social, Legal, Recreational, Religious	30	3.98%	40	4.25%
Writers, Entertainers, Athletes	42	5.57%	33	3.50%
Photographers, Painters, Artists	8	1.06%	8	0.85%
Health Technicians	15	1.99%	25	2.65%
Engineering, Science Technicians	7	0.93%	9	0.96%
Other Technicians	16	2.12%	12	1.27%
Sales Occupations	159	21.09%	218	23.14%
Administrative Support Occupations	399	52.92%	446	47.35%
Private Household Service Occupations	19	2.52%	20	2.12%
Law Enforcement and Guards	5	0.66%	5	0.53%
Food Service Occupations	103	13.66%	143	15.18%
Health Service Occupations	35	4.64%	68	7.22%

Table 9 (continued). Prevalence of ever employment in occupational groups among breast cancer cases and control women.

	Cases		Controls	
Occupational Group	n	Prevalence	n	Prevalence
Cleaning Service, Except Household	21	2.79%	20	2.12%
Personal Service Occupations	44	5.84%	67	7.11%
Farmers & Farm Managers	3	0.40%	3	0.32%
Farm & Nursery Workers & Gardeners	3	0.40%	9	0.96%
Other Agricultural Occupations	2	0.27%	8	0.85%
Forestry & Logging Occupations	2	0.27%	4	0.42%
Fishers, Hunters & Trappers	0	0.00%	1	0.11%
Vehicle Mechanics	3	0.40%	2	0.21%
Electrical/Electronic Equip. Repairers	3	0.40%	4	0.42%
Miscellaneous Mechanics & Repairers	2	0.27%	2	0.21%
Carpenters	1	0.13%	2	0.21%
Electricians	2	0.27%	2	0.21%
Painters	3	0.40%	3	0.32%
Plumbers, Pipefitters, & Steamfitters	1	0.13%	0	0.00%
Roofers and Pavers	0	0.00%	1	0.11%
Other Construction Occupations	2	0.27%	2	0.21%
Supervisors, Production Occupations	2	0.27%	1	0.11%
Precision Metal Workers	0	0.00%	6	0.64%
Precision Textile Workers	11	1.46%	4	0.42%
Precision Workers, Assorted Materials	6	0.80%	2	0.21%
Precision Food Production Occupations	3	0.40%	3	0.32%
Inspectors, Testers, & Calibrators	7	0.93%	9	0.96%
Metal & Plastic Working Machine Oper.	1	0.13%	7	0.74%
Metal & Plastic Processing Mach. Oper.	0	0.00%	2	0.21%
Woodworking Machine Operator	2	0.27%	1	0.11%
Printing Machine Operators	8	1.06%	1	0.11%
Textile Machine Operators	14	1.86%	12	1.27%
Other Machine Operators	16	2.12%	18	1.91%
Welders & Cutters	1	0.13%	1	0.11%
Other Hand Working Occupations	21	2.79%	19	2.02%
Motor Vehicle Operators	16	2.12%	12	1.27%
Material Moving Equipment Operators	0	0.00%	3	0.32%
Handlers, Cleaners & Laborers	16	2.12%	13	1.38%

Table 10. Prevalence of ever employment in industry groups among breast cancer cases and control women.

	Cases		Controls	
Industry Group	n	Prevalence	n	Prevalence
Agriculture	12	1.59%	24	2.55%
Forestry	4	0.53%	3	0.32%
Fishing, Hunting, & Trapping	3	0.40%	3	0.32%
Mining & Extraction	1	0.13%	1	0.11%
Construction	20	2.65%	38	4.03%
Food Product Manufacture	25	3.32%	19	2.02%
Textile Product Manufacture	23	3.05%	20	2.12%
Paper Product Manufacture	8	1.06%	4	0.42%
Printing & Publishing	24	3.18%	21	2.23%
Chemical Product Manufacture	10	1.33%	12	1.27%
Petroleum/Coal Refining & Product Mfg.	3	0.40%	0	0.00%
Rubber & Plastic Product Manufacture	3	0.40%	4	0.42%
Leather Product Manufacture	2	0.27%	3	0.32%
Lumber & Wood Product Manufacture	13	1.72%	9	0.96%
Furniture & Fixtures Manufacture	3	0.40%	1	0.11%
Stone, Glass, Concrete Product Mfg.	6	0.80%	4	0.42%
Primary Metal Industries	2	0.27%	5	0.53%
Metal Product Manufacture	2	0.27%	7	0.74%
Machinery Mfg., Except Electric	8	1.06%	16	1.70%
Electrical Product Manufacture	17	2.25%	20	2.12%
Motor Vehicle Manufacture	4	0.53%	1	0.11%
Aircraft, Aerospace & Parts Mfg.	43	5.70%	58	6.16%
Ship & Boat Manufacture & Repair	7	0.93%	6	0.64%
Miscellaneous Manufacture	18	2.39%	23	2.44%
Transportation	46	6.10%	58	6.16%
Communication & Utilities	43	5.70%	49	5.20%
Wholesale & Retail Trade	267	35.41%	344	36.52%
Financial, Insurance & Real Estate	156	20.69%	173	18.37%
Business Services	51	6.76%	63	6.69%
Repair Services	6	0.80%	6	0.64%
Personal Services	69	9.15%	74	7.86%
Entertainment & Recreational Services	36	4.77%	31	3.29%
Health Care Services	147	19.50%	221	23.46%
Professional & Related Services	267	35.41%	278	29.51%
Public Administration	69	9.15%	88	9.34%

Occupational exposure to electromagnetic fields was assessed using two strategies (Tables 11 and 12). The first the was the scheme proposed by Coogan et al (24) for a study of breast cancer among women in which four exposure categories were used for exposure to 60-hertz magnetic fields (background, low, medium, and high). The second was the scheme proposed by Demers et al (25) for a study of breast cancer among men. This latter scheme placed potentially exposed jobs which have been identified in previous studies into five categories (electrical trades and related, electrical equipment repair, communications and broadcasting, electrical and electronic engineers and technicians, and welders).

Table 11. Occupational exposure to electromagnetic fields among breast cancer cases and controls aged 45 years or less (based on Coogan [24] classification).

	Cases (n=754)		Controls (n=942)	
EMF exposure	n	%	n	%
None (background)	567	75.2	729	77.4
Low	125	16.6	142	15.1
Medium	28	3.7	38	4.0
High	34	4.5	33	3.5

Table 12. Occupational exposure to electromagnetic fields among breast cancer cases and control women aged 45 years or less (based on Demers [25] classification).

	Cases (n=754)		Controls (n=942)	
EMF exposure	n	%	n	%
None (background)	741	98.3	926	98.3
Electrical trades and related work	2	0.3	2	0.2
Electrical equipment repair	1	0.1	3	0.3
Communications and broadcasting	4	0.5	5	0.5
Electrical / electronic engineers and technicians	5	0.7	5	0.5
Welders	1	0.1	1	0.1

Occupational physical activity was assessed using the same methods as those used by Coogan et al (26) for a study of breast cancer among women (Table 13). Each job was classified by the physical demands of the job using the ratings developed by the US Department of Labor (27). Five strength categories were used (sedentary, light, medium, heavy, very heavy). These categories were developed by the U.S. Employment Service (USES) Occupational Analysis Program and were based primarily on the body position, weight of objects, and force needed to perform jobs.

Table 13. Level of strength required/physical demand of reported jobs among breast cancer cases and control women aged 45 years or less (based on ratings developed by the US Department of Labor [27]).

	Cases (n=754)		Controls (n=942)	
Physical activity level*	n	%	n	%
Sedentary	135	17.9	158	16.8
Light	392	52.0	478	50.7
Medium	169	22.4	210	22.3
Heavy	58	7.7	96	10.2

*: no cases or controls reported jobs associated with a 'very heavy' strength category.

Logistic regression (STATA™ version 5.0) was used to determine odds ratios as estimates of the relative risk for breast cancer associated with employment in various occupations and industries, occupational exposure to electromagnetic fields (EMF), and occupational exposure to strenuous physical activity. Trends were evaluated using the likelihood ratio statistic.

Conclusions

Of the four analyses funded by the U.S. Army Medical Research and Materiel Command under DAMD-14-96-1-6118, the conclusions from the three completed analyses are as follows:

1. We found a small elevation in breast cancer risk associated with any use of hair coloring; however, exclusive use of one of the four types of hair coloring application was not associated with elevated risks for breast cancer among reproductive-age women. It is not clear why we found an elevated breast cancer risk associated with any use of one of the four types of hair coloring application. Elevations in risk were not restricted to one type of hair coloring application (for example rinses or frosting) in combination with the other types. Furthermore, we found no increasing risk with increased frequency of use or any consistent pattern of risk associated with the timing of use. And finally, hair spray use was not associated with an elevation in breast cancer risk. The lack of an association between exclusive use of a single type of hair coloring application and breast cancer risk, particularly among the large number of women who exclusively used semi-permanent and permanent dyes, argues that hair coloring application does not influence breast cancer risk among reproductive-age women. However, we did see a small elevation in breast cancer risk associated with the use of any hair coloring. Thus, we cannot preclude the possibility that there may be a small elevation in breast cancer risk associated with hair coloring application.
2. Our results suggest that among multiparous women of the same age, parity, and age at first term birth, there is no increased risk of breast cancer for those who had their last term pregnancy late in their reproductive life compared to women who had their last term pregnancy earlier. Our results also suggest that there is no consistent pattern of an elevated risk for breast cancer for several years following a term birth for women who have another pregnancy compared to women of the same age who do not have an additional pregnancy.
3. No conclusions are available at this time concerning the relation between occupation and breast cancer risk in young women since full study results were not presented pending review by the other investigators.

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Bibliography of Grant Related Publications/Abstracts

Publications:

none

Abstracts:

1. Cook LS, Malone KE, Daling JR, McKnight B, Voigt L, Weiss NS. Risk of breast cancer among young women: relationship to a recent term pregnancy. Department of Defense Breast Cancer Research Program's 'Era of Hope' meeting, Washington DC, October 1997.

2. Cook LS, Malone KE, Daling JR, Voigt LF, Weiss NS. Hair coloring and the risk of breast cancer in young women. 30th Annual Meeting of the Society for Epidemiological Research, Edmonton, Alberta, June 12- 14, 1997.

Personnel

Linda S. Cook, Ph.D.
The U.S. Army Medical Research and Materiel Command under DAMD-14-96-1-6118 provided funding for two years of postdoctoral training to support Dr. Cook's work on analyses investigating risk factors for breast cancer. This funding provided salary support and covered travel costs to two national meetings. No other personnel received pay from the negotiated effort.

Appendix:

Annual Report Review,
USAMRMC FY 95 Breast Cancer Research Program
Reporting Period: 1 July 1996 – 30 June 1997

ANNUAL REPORT REVIEW
USAMRMC FY 95 BREAST CANCER RESEARCH PROGRAM

Grant/Contract/MIPR No.:	DAMD17-96-1-6118
Principal Investigator:	Linda S. Cook, Ph.D.
Institution:	Fred Hutchinson Cancer Research Center Seattle, Washington 98104-2092
Report Title:	Post-Doctoral Training: Case-Control Analysis of Breast Cancer
Report Type:	Annual
Date of Report:	July 1997
Reporting Period:	1 July 1996 - 30 June 1997

SUMMARY REVIEW: Many inconsistent and inconclusive associations between factors suspected to be related to breast cancer risk have been documented. The overall goal of this funding effort is to examine the relationship between various occupational, reproductive, and lifestyle exposures and breast cancer.

During the first year of the grant, analysis of hair dye use among young women and its association with increased breast cancer risk was explored. Eligible women were identified through the Cancer Surveillance System in Washington state. The following eligibility criteria were imposed: (1) Caucasian; (2) residing in one of three counties in western Washington; (3) diagnosed with *in-situ* or invasive breast cancer between 1983 and 1990; and (4) born in 1945 or later. A total of 844 women who met the eligibility criteria participated in the analysis. Nine hundred sixty women of similar age who were randomly selected served as controls. Extensive information has been gathered by in-person interview, including demographic, lifestyle, reproductive, and medical histories. In addition, the women provided information on personal hair coloring and hair spray applications. Hair coloring applications were categorized as follows: (1) rinses (coloring applied to the hair that washed out in the next shampoo); (2) semi-permanent dyes (coloring that remained over multiple washings) or permanent dyes; (3) bleaching then dyeing with either semi-permanent or permanent dyes; or (4) frosting/tipping (partial coloring of hair). Women who reported any hair coloring application (529 for cases and 542 for controls) were compared to those women who never used hair coloring applications (315 for cases and 418 for controls). A modest elevation in breast cancer risk was observed in those women who reported any use of hair coloring. Exclusive use of a single type of hair coloring

application could not account for the increased risk. However, there is not an elevated risk for breast cancer associated with increased frequency of hair coloring applications or with the timing of use. Furthermore, use of hair spray and frequency of application did not increase the risk of breast cancer.

Analysis of recent term pregnancy and its association with breast cancer risk was also explored. Eligible women were identified through a population-based cancer registry of western Washington state. The following eligibility criteria were imposed: (1) between ages 21 and 45; (2) diagnosed with *in-situ* or invasive breast cancer between January 1, 1983 and April 30, 1990; and (3) residing in one of three metropolitan counties in western Washington. Eight hundred forty-five women met the eligibility criteria. Nine hundred sixty women of similar age and residence were randomly selected to serve as controls. Information was gathered on pregnancies, reproductive factors, and potential breast cancer risk factors. The impact of the last birth occurring earlier or later in life was compared among 486 multiparous women and 494 controls. A lack of an association for risk of breast cancer and the time since the last birth was observed. Moreover, the impact of an additional birth on the risk of breast cancer was assessed. Women of any given parity were compared to women with one less childbirth. Comparisons were made for women of different ages. However, no clear pattern of breast cancer risk for women with an additional birth was remarked.

Project elements that are currently under investigation include evaluating (1) the impact of breast feeding on breast cancer risk and (2) occupational history and the risk of breast cancer.

FORMAT/EDITORIAL ISSUES: This report conforms to USAMRMC format requirements.

CONTRACTUAL ISSUES: Information is provided in this first annual report that supports the following:

Task 1	Months 1-5	Completed
Task 2	Months 6-14	Partially completed
Task 3	Months 15-24	Partially completed
Task 4	Months 25-36	Studies initiated

This report is in general compliance with the goals stated in the Statement of Work (SOW).

TECHNICAL ISSUES: The report should include a bibliography of any publications resulting from work supported by the USAMRMC.

SPECIFIC DISCREPANCIES AND RECOMMENDATIONS: This annual report is acceptable as submitted. It should be noted that substantial progress has been made in fulfilling items listed in the SOW.

KEY ACCOMPLISHMENTS:

- A modest elevation in breast cancer risk was observed in women who reported any use of hair coloring. However, exclusive use of a single type of hair coloring application could not account for the increased risk. Furthermore, use of hair spray and frequency of application did not increase the risk of breast cancer.

REVISED DRAFT REQUIRED: **YES**___ **NO** x